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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12N 15/12, C07K 14/705, C12N 5/10, C07K 16/28, G01N 33/563, 33/50, A61K 31/70, A01K 67/00

A1

(11) International Publication Number: WO 98/53062

(43) International Publication Date: 26 November 1998 (26.11.98)

(21) International Application Number: PCT/CA98/00487

(22) International Filing Date: 22 May 1998 (22.05.98)

(30) Priority Data:
08/861,747 22 May 1997 (22.05.97) US

(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application
US 08/861,747 (CIP)
Filed on 22 May 1997 (22.05.97)

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(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
With amended claims.

(54) Title: A HUMAN EDG-6 RECEPTOR HOMOLOGUE

(57) Abstract

An isolated nucleic acid sequence coding for an amino acid sequence for a novel human EDG-6 receptor homologue is provided. Also provided are purified human EDG-6 receptor polypeptides derived from the nucleic acid and methods and transgenic animals therefor.

A HUMAN EDG-6 RECEPTOR HOMOLOGUE

FIELD OF THE INVENTION

The present invention is in the field of molecular biology; more particularly, the present invention describes a nucleic acid sequence and an amino acid sequence for a novel human EDG-6 receptor homologue.

BACKGROUND OF THE INVENTION

The family of edg (endothelial differentiation gene) receptors are commonly grouped with orphan receptors because their endogenous ligands are not known (for example see Hla, T. and Maciag, T. (1990) J. Biol. Chem. 265:9308-13; US patent 5,585,476). Recently, however, lysophospatidic acid (LPA) has been demonstrated to be the endogenous ligand for the edg-2 receptor (Hecht et al. (1996) J. Cell. Biol. 135: 1071-1083; An et al. (1997) Biochem. Biophys. Res. Comm. 213: 619-622).

The edg family of receptors are seven transmembrane G protein coupled receptors (T7Gs). T7Gs are so named because of their seven hydrophobic domains which span the plasma membrane and form a bundle of antiparallel α helices. These transmembrane segments (TMS) are designated by roman numerals I-VII and account for structural and functional features of the receptor. In most cases, the bundle of helices forms a binding pocket; however, when the binding site must accommodate more bulky molecules, the extracellular N-terminal segment or one or more of the three extracellular loops participate in binding and in subsequent induction of conformational change in intracellular portions of the receptor. The activated receptor, in turn, interacts with an intracellular G-protein complex which mediates further intracellular signaling activities generally the production of second messengers such as cyclic AMP (cAMP), phospholipase C, inositol triphosphate or ion channel proteins.

T7G receptors are expressed and activated during numerous developmental and disease processes. Identification of a novel T7G receptor provides the opportunity to diagnose or intervene in such processes, and the receptor can be used in screening assays to identify physiological or pharmaceutical molecules which trigger, prolong or inhibit its activity.

SUMMARY OF THE INVENTION

The invention provides a unique nucleotide sequence which encodes a novel human EDG-6 receptor homologue (HEDG). Herein, the nucleotide sequence encoding HEDG is designated hedg. Thus, the invention provides an isolated nucleic acid molecule wherein the nucleic acid molecule encodes a polypeptide having an amino acid sequence as shown in SEQ. ID NO:2.

In another embodiment, the invention provides an isolated nucleic acid molecule having a nucleotide sequence as shown in SEQ. ID NO:1.

In yet another embodiment, the invention provides a nucleic acid molecule which is anti-sense to the molecules indicated above.

In a further embodiment, the invention provides for expression vectors, probes and DNA constructs based on the polynucleotides mentioned above.

In another embodiment, the invention provides for a purified polypeptide having the amino acid sequence as shown in SEQ. ID NO:2.

The invention also provides for antibodies specific to the above polypeptide.

In another embodiment, the invention provides for methods of purifying and assaying polypeptides as indicated above.

In a further embodiment, the invention provides for transgenic animals which include the nucleotide sequence of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A and 1B shows the alignment of the nucleic acid sequence (coding region of SEQ. ID NO: 1) and amino acid sequence (SEQ. ID NO:2) for HEDG.

Figure 2 displays the nucleic acid sequence (SEQ. ID NO:3) of a cDNA encoding HEDG.

DETAILED DESCRIPTION OF THE INVENTION

As used herein and designated by the upper case abbreviation, HEDG, refers to an EDG-6 receptor homologue in either naturally occurring or synthetic form and active fragments thereof which have the amino acid sequence of SEQ. ID NO:2. In one

embodiment, the polypeptide HEDG is encoded by mRNAs transcribed from the cDNA, as designated by the lower case abbreviation, hedg, of SEQ. ID NO:1.

The novel human EDG-6 receptor homologue, HEDG, was cloned and isolated from a human kidney proximal tubule cDNA library. It shows 52.9% identity to human edg-2 (WO 97/00952).

An "oligonucleotide" is a stretch of nucleotide residues which has a sufficient number of bases to be used as an oligomer, amplimer or probe in a polymerase chain reaction (PCR). Oligonucleotides are prepared from genomic or cDNA sequence and are used to amplify, reveal or confirm the presence of a similar DNA or RNA in a particular cell or tissue. Oligonucleotides or oligomers comprise portions of a DNA sequence having at least about 10 nucleotides and as many as about 35 nucleotides, preferably about 25 nucleotides.

"Probes" may be derived from naturally occurring or recombinant single - or double - stranded nucleic acids or be chemically synthesized. They are useful in detecting the presence of identical or similar sequences.

A "portion" or "fragment" of a polynucleotide or nucleic acid comprises all or any part of the nucleotide sequence having fewer nucleotides than about 6 kb, preferably fewer than about 1 kb which can be used as a probe. Such probes may be labeled with reporter molecules using nick translation, Klenow fill-in reaction, PCR or other methods well known in the art. After optimizing reaction conditions to eliminate false positives, nucleic acid probes may be used in Southern, Northern or in situ hybridizations to determine whether DNA or RNA encoding HEDG is present in a cell type, tissue, or organ.

"Reporter" molecules are those radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents which associate with, establish the presence of, and may allow quantification of a particular nucleotide or amino acid sequence.

"Recombinant nucleotide variants" encoding HEDG may be synthesized by making use of the "redundancy" in the genetic code. Various codon substitutions, such as the silent changes which produce specific restriction sites or codon usage-specific mutations, may be introduced to optimize cloning into a plasmid or viral vector or expression in a particular prokaryotic or eukaryotic host system, respectively.

"Chimeric" molecules may be constructed by introducing all or part of the nucleotide sequence of this invention into a vector containing additional nucleic acid sequence which might be expected to change any one (or more than one) of the following

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: MUNROE, Donald G.
VYAS, Tejal B.

(ii) TITLE OF INVENTION: A HUMAN EDG-6 RECEPTOR HOMOLOG

(iii) NUMBER OF SEQUENCES: 7

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(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: US 08/861,747
(B) FILING DATE: 22-MAY-1997
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:
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(B) REGISTRATION NUMBER: 41,092
(C) REFERENCE/DOCKET NUMBER: P8074-7003

(ix) TELECOMMUNICATION INFORMATION:
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(B) TELEFAX: (202) 638-4810

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1761 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

CGCTCCCGCC GCAGTCGCCG GGCCATGGGC CTCGAGCCCG CCCCGAACCC CCGCGAGCCC 60

GCCTTGTCTG CGGCGTGACT GGAGGCCCAG ATGGTCATCA TGGGCCAGTG CTACTACAAC 120

GAGACCATCG GTTTCTTCTA TAACAACAGT GGCAAAGAGC TCAGCTCCCA CTGGCGGCCC 180

AAGGATGTGG TCGTGGTGGC ACTGGGGCTG ACCGTCAGCG TGCTGGTGCT GCTGACCAAT 240

CTGCTGGTCA TAGCAGCCAT CGCCTCCAAC CGCCGCTTCC ACCAGCCCAT CTACTACCTG 300

CTCGGCAATC TGGCCGCGGC TGACCTCTTC GCGGGCGTGG CCTACCTCTT CCTCATGTTC 360

CACACTGGTC CCCGCACAGC CCGACTTTCA CTTGAGGGCT GGTTCCTGCG GCAGGGCTTG 420

CTGGACACAA GCCTCACTGC GTCGGTGGCC ACACTGCTGG CCATCGCCGT GGAACGGCAC 480

CGCAGTGTGA TGGCCGTACA GTTGCACAGC CGCCTGCCCC GTGGCCGCGT GGTCATGCTC 540

ATTGTGGGCG TGTGGGTGGC TGCCCTGGGC CTGGGGCTGT TGCCTGCCCA CTCCTGGCAC 600

TGCCTCTGTG CCCTGGACCG CTGCTCACGC ATGGCACCCC TGCTCAGCCG CTCCTATTTG 660

GCCGTCTGGG CTCTGTCGAG CCTGCTTGTC TTCCTGCTCA TGGTGGCTGT GTACACCCGC 720

ATTTTTTTAT ACGTGCGGCG GCGAGTGCAG CGCATGGCAG AGCATGTCAG CTGCCACCCC 780

CGCTACCGAG AGACCACGCT CAGCCTGGTC AAGACTGTTG TCATCATCCT GGGGGCGTTC 840

GTGGTCTGCT GGACACCAGG CCAGGTGGTA CTGCTCCTGG ATGGTTTAGG CTGTGAGTCC 900

TGCAATGTCC TGGCTGTAGA AAAGTACTTC CTACTGTTGG CCGAGGCCAA CTCACTGGTC 960

AATGCTGCTG TGTACTCTTG CCGAGATGCT GAGATGCGCC GCACCTTCCG CCGCCTTCTC 1020

TGCTGCGCGT GCCTCCGCCA GCCCACCCGC GAGTCTGTCC ACTATACATC CTCTGCCCAG 1080

GGAGGTGCCA GCACTCGCAT CATGCTTCCC GAGAACGGCC ACCCACTGAT GGACTCCACC 1140

CTTTAGCTAC CTTGAACTTC AGCGGTACGC GGCAAGCAAC AAATCCACAG CCCCTGATGA 1200

CTTGTGGGTG CTCCTGGCTC AACCCAACCA ACAGGACTGA CTGACCGGCA GGACAAGGTC 1260

TGGCATGGCA CAGCACCACT GCCAGGCCTC CCCAGGCACA CCACTCTGCC CAGGGAATGG 1320

GGGCTTTGGG TCATCTCCCA CTGCCTGGGG GAGTCAGATG GGGTGCAGGA ATCTGGCTCT 1380

TCAGCCATCC CAGGTTTAGG GGGTTTGTAA CAGACATTAT TCTGTTTTCA CTGCGTATCC 1440

TTGGTAAGCC CTGTGGACTG GTTCCTGCTG TGTGATGCTG AGGGTTTTAA GGTGGGGAGA 1500

GATAAGGGCT CTCTCGGGCC ATGCTACCCG GTATGACTGG GTAATGAGGA CAGACTGTGG 1560

ACACCCCATY TACCTGAGTC TGATTCTTTA GCAGCAGAGA CTGAGGGGTG CAGAGTGTGA 1620

GCTGGGAAAG GTTTGTGGCT CCTTGCAGCC TCCAGGGACT GGCCTGTCCC CGATAGAATT 1680

GAAGCAGTCC ACGGGGAGGG GATGATACAA GGAGTAAACC TTTCTTTACA CTCTGAGGTC 1740

TCCAAAACAT TTGTTGTTAT C 1761

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 351 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

```
Met Val Ile Met Gly Gln Cys Tyr Tyr Asn Glu Thr Ile Gly Phe Phe
1               5                  10                  15

Tyr Asn Asn Ser Gly Lys Glu Leu Ser Ser His Trp Arg Pro Lys Asp
            20                  25                  30

Val Val Val Val Ala Leu Gly Leu Thr Val Ser Val Leu Val Leu Leu
        35                  40                  45

Thr Asn Leu Leu Val Ile Ala Ala Ile Ala Ser Asn Arg Arg Phe His
    50                  55                  60

Gln Pro Ile Tyr Tyr Leu Leu Gly Asn Leu Ala Ala Ala Asp Leu Phe
65                  70                  75                  80

Ala Gly Val Ala Tyr Leu Phe Leu Met Phe His Thr Gly Pro Arg Thr
                85                  90                  95

Ala Arg Leu Ser Leu Glu Gly Trp Phe Leu Arg Gln Gly Leu Leu Asp
            100                 105                 110

Thr Ser Leu Thr Ala Ser Val Ala Thr Leu Leu Ala Ile Ala Val Glu
        115                 120                 125

Arg His Arg Ser Val Met Ala Val Gln Leu His Ser Arg Leu Pro Arg
    130                 135                 140

Gly Arg Val Val Met Leu Ile Val Gly Val Trp Val Ala Ala Leu Gly
145                 150                 155                 160

Leu Gly Leu Leu Pro Ala His Ser Trp His Cys Leu Cys Ala Leu Asp
                165                 170                 175

Arg Cys Ser Arg Met Ala Pro Leu Leu Ser Arg Ser Tyr Leu Ala Val
            180                 185                 190

Trp Ala Leu Ser Ser Leu Leu Val Phe Leu Leu Met Val Ala Val Tyr
        195                 200                 205

Thr Arg Ile Phe Leu Tyr Val Arg Arg Arg Val Gln Arg Met Ala Glu
    210                 215                 220

His Val Ser Cys His Pro Arg Tyr Arg Glu Thr Thr Leu Ser Leu Val
225                 230                 235                 240

Lys Thr Val Val Ile Ile Leu Gly Ala Phe Val Val Cys Trp Thr Pro
                245                 250                 255

Gly Gln Val Val Leu Leu Leu Asp Gly Leu Gly Cys Glu Ser Cys Asn
            260                 265                 270

Val Leu Ala Val Glu Lys Tyr Phe Leu Leu Leu Ala Glu Ala Asn Ser
        275                 280                 285

Leu Val Asn Ala Ala Val Tyr Ser Cys Arg Asp Ala Glu Met Arg Arg
    290                 295                 300

Thr Phe Arg Arg Leu Leu Cys Cys Ala Cys Leu Arg Gln Pro Thr Arg
305                 310                 315                 320
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Glu Ser Val His Tyr Thr Ser Ser Ala Gln Gly Gly Ala Ser Thr Arg
325 330 335

Ile Met Leu Pro Glu Asn Gly His Pro Leu Met Asp Ser Thr Leu
340 345 350

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1889 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

TTACGAATTA ATACGATCAC TATAGGGAGA CCAAGCTTGG TACCGAGCTC GGATCCACTA 60

GTAACGGCCG CCAGTGTGGG GAATTCCGCT CCCGCCGCAG TCGCCGGGCC ATGGGCCTCG 120

AGCCCGCCCC GAACCCCCGC GAGCCCGCCT TGTCTGCGGC GTGACTGGAG GCCCAGATGG 180

TCATCATGGG CCAGTGCTAC TACAACGAGA CCATCGGTTT CTTCTATAAC AACAGTGGCA 240

AAGAGCTCAG CTCCCACTGG CGGCCCAAGG ATGTGGTCGT GGTGGCACTG GGGCTGACCG 300

TCAGCGTGCT GGTGCTGCTG ACCAATCTGC TGGTCATAGC AGCCATCGCC TCCAACCGCC 360

GCTTCCACCA GCCCATCTAC TACCTGCTCG GCAATCTGGC CGCGGCTGAC CTCTTCGCGG 420

GCGTGGCCTA CCTCTTCCTC ATGTTCCACA CTGGTCCCCG CACAGCCCGA CTTTCACTTG 480

AGGGCTGGTT CCTGCGGCAG GGCTTGCTGG ACACAAGCCT CACTGCGTCG GTGGCCACAC 540

TGCTGGCCAT CGCCGTGGAA CGGCACCGCA GTGTGATGGC CGTACAGTTG CACAGCCGCC 600

TGCCCCGTGG CCGCGTGGTC ATGCTCATTG TGGGCGTGTG GGTGGCTGCC CTGGGCCTGG 660

GGCTGTTGCC TGCCCACTCC TGGCACTGCC TCTGTGCCCT GGACCGCTGC TCACGCATGG 720

CACCCCTGCT CAGCCGCTCC TATTTGGCCG TCTGGGCTCT GTCGAGCCTG CTTGTCTTCC 780

TGCTCATGGT GGCTGTGTAC ACCCGCATTT TTTTATACGT GCGGCGGCGA GTGCAGCGCA 840

TGGCAGAGCA TGTCAGCTGC CACCCCCGCT ACCGAGAGAC CACGCTCAGC CTGGTCAAGA 900

CTGTTGTCAT CATCCTGGGG GCGTTCGTGG TCTGCTGGAC ACCAGGCCAG GTGGTACTGC 960

TCCTGGATGG TTTAGGCTGT GAGTCCTGCA ATGTCCTGGC TGTAGAAAAG TACTTCCTAC 1020

TGTTGGCCGA GGCCAACTCA CTGGTCAATG CTGCTGTGTA CTCTTGCCGA GATGCTGAGA 1080

TGCGCCGCAC CTTCCGCCGC CTTCTCTGCT GCGCGTGCCT CCGCCAGCCC ACCCGCGAGT 1140

CTGTCCACTA TACATCCTCT GCCCAGGGAG GTGCCAGCAC TCGCATCATG CTTCCCGAGA 1200

ACGGCCACCC ACTGATGGAC TCCACCCTTT AGCTACCTTG AACTTCAGCG GTACGCGGCA 1260

AGCAACAAAT CCACAGCCCC TGATGACTTG TGGGTGCTCC TGGCTCAACC CAACCAACAG 1320

GACTGACTGA CCGGCAGGAC AAGGTCTGGC ATGGCACAGC ACCACTGCCA GGCCTCCCCA 1380

GGCACACCAC TCTGCCCAGG GAATGGGGGC TTTGGGTCAT CTCCCACTGC CTGGGGGAGT 1440

CAGATGGGGT GCAGGAATCT GGCTCTTCAG CCATCCCAGG TTTAGGGGGT TTGTAACAGA 1500

CATTATTCTG TTTTCACTGC GTATCCTTGG TAAGCCCTGT GGACTGGTTC CTGCTGTGTG 1560

ATGCTGAGGG TTTTAAGGTG GGGAGAGATA AGGGCTCTCT CGGGCCATGC TACCCGGTAT 1620

GACTGGGTAA TGAGGACAGA CTGTGGACAC CCCATYTACC TGAGTCTGAT TCTTTAGCAG 1680

CAGAGACTGA GGGGTGCAGA GTGTGAGCTG GGAAAGGTTT GTGGCTCCTT GCAGCCTCCA 1740

GGGACTGGCC TGTCCCCGAT AGAATTGAAG CAGTCCACGG GGAGGGGATG ATACAAGGAG 1800

TAAACCTTTC TTTACACTCT GAGGTCTCCA AAACATTTGT TGTTATCAAA AAAAAAAAAA 1860

AAAAAAAAAA AAAAAAAAAA AGCGGCCGC 1889

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

GGTGGTACTG CTCCTGGATG GTTTAG 26

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CGGAGGCACG CGCAGCAGAG AAGA 24

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

TAGAGAACCC ACTGCTTAC 19

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CCCAGAATAG AATGACACC 19

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. An isolated nucleic acid molecule wherein said nucleic acid molecule encodes a polypeptide having an amino acid sequence as shown in SEQ. ID NO:2.

2. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid is DNA.

3. The isolated nucleic acid of claim 2 wherein said nucleic acid is selected from the group consisting of:

a) the nucleotide sequence as shown in SEQ. ID NO:1;

b) nucleotide sequences that hybridize to SEQ. ID NO:1or to its complementary strand;

c) nucleotide sequences that differ from SEQ. ID NO:1 and from the nucleotide sequences of (b) in codon sequence due the degeneracy of the genetic code.

4. The isolated nucleic acid of claim 2 wherein said nucleic acid includes the nucleotide sequence as shown in SEQ. ID NO:1.

5. The isolated nucleic acid of claim 1 wherein said nucleic acid is RNA.

6. An isolated nucleic acid which is anti-sense to a nucleic acid as claimed in claim 1.

7. An isolated nucleic acid which is anti-sense to a nucleic acid as claimed in claim 3.

8. An isolated nucleic acid which is anti-sense to a nucleic acid as claimed in claim 4

9. The isolated nucleic acid of claim 1 which is an RNA anti-sense sequence.

10. A DNA construct comprising the following operably linked elements:

a) a transcriptional promoter;

b) a DNA sequence including the nucleotide sequence as shown in SEQ. ID NO:1; and,

c) a transcriptional terminator.

11. The DNA construct of claim 10 wherein said DNA sequence encodes the polypeptide of SEQ. ID NO:2.

12. A recombinant expression vector suitable for transformation of a host cell comprising a nucleic acid as claimed in claim 1 and a regulatory sequence operatively linked to said nucleic acid.

13. A recombinant expression vector suitable for transformation of a host cell comprising a DNA molecule having a nucleotide sequence as shown in SEQ. ID NO:1 and a regulatory sequence operatively linked to said DNA molecule.

14. The recombinant expression vector of claim 13 wherein the DNA molecule is operatively linked to the regulatory sequence to allow expression of an RNA molecule which is anti-sense to a nucleotide sequence as shown in SEQ. ID NO:1.

15. A transformed cell including a recombinant expression vector as claimed in claim 12.

16. A transformed cell including a recombinant expression vector as claimed in claim 13.

17. A method for preparing an isolated protein having an amino acid sequence as shown in SEQ. ID NO:2 said method comprising culturing a transformed cell including a recombinant expression vector as claimed in claim 13 in a suitable medium until the protein is formed and isolating said protein.

18. The polypeptide expressed by the expression vector of claim13.

19. pharmaceutical composition comprising the antisense molecule of claim 3 and a pharmaceutically acceptable carrier.

20. A probe comprising an oligonucleotide of the nucleic acid as shown in SEQ. ID NO:1 capable of specifically hybridizing with a gene which encodes a protein having an amino acid sequence as shown in SEQ. ID NO:2 or allelic and species variants thereof.

21. An isolated polypeptide having the amino acid sequence as shown in SEQ. ID NO:2.

22. A purified polyclonal antibody specific for the amino acid sequence as shown in SEQ. ID NO:2.

23. The purified polyclonal antibody of claim 22 wherein said antibody is specific for an extracellular epitope of the protein having the amino acid sequence as shown in SEQ. ID NO:2.

24. The purified polyclonal antibody of claim 22 wherein the antibody is labeled.

25. A monoclonal antibody specific for the amino acid sequence as shown in SEQ. ID NO:2.

26. The monoclonal antibody of claim 25 wherein said antibody is specific for an extracellular epitope of the protein having the amino acid sequence as shown in SEQ. ID NO:2.

27. The monoclonal antibody of claim 25 wherein the antibody is labeled.

28. The method for determining the presence of a protein having an amino acid sequence as shown in SEQ. ID NO:2 in a biological sample, the method comprising the steps of:

a) incubating the sample with a monoclonal antibody or purified polyclonal antibody which specifically binds to an epitope of said protein under conditions sufficient for the formation of an immune complex; and,

b) determining the presence of said immune complex.

29. The method of claim 28 wherein the monoclonal or purified polyclonal antibody is labeled.

30. A method of purifying a protein having the amino acid sequence as shown in SEQ. ID NO:2, the method including an immunoaffinity chromatography process wherein a monoclonal antibody or a purified polyclonal antibody specific to an epitope of said protein is immobilized on the chromatography resin.

31. A method of screening a molecule which ligates to the protein having the amino acid sequence as shown in SEQ. ID NO:2 comprising a signal transduction assay.

32. The method of claim 31, wherein the protein is a G protein coupled receptor, the method comprising the following steps:

a) co-transfecting into a suitable cell of a plasmid including a reporter gene and an expression plasmid coding for said protein;

b) expressing said protein;

c) treating said cell with serum starvation to reduce mitogenic activity;

d) applying said molecule which ligates to said protein in a serum free medium; and,

e) measuring the activity of the reporter.

33. A transgenic animal expressing a first transgene coding for a protein having an amino acid sequence as shown in SEQ. ID NO:2.

34. The transgenic animal of claim 33 wherein said first transgene comprises a polynucleotide having a nucleotide sequence as shown in SEQ. ID NO:1.

35. A transgenic animal as claimed in claim 33 further including a second transgene coding for an inducible promoter for said first transgene.

36. A transgenic animal as claimed in claim 33 further including a second transgene coding for a tissue specific regulatory element for regulating the expression of said first transgene.

AMENDED CLAIMS
[received by the International Bureau on 6 November 1998 (06.11.98); original claims 1-36 replaced by amended claims 1-22 (3 pages)].

1. An isolated nucleic acid molecule wherein the molecule is selected from the group consisting of :

a) a molecule having a nucleic acid sequence as shown in SEQ. ID. NO: 1; and

b) hybridizing nucleic acid molecules that hybridize to a molecule having a nucleic acid sequence as shown in SEQ. ID NO:1 or to complementary strands thereof, said hybridizing nucleic acid molecules having at least 40% homology with a molecule having a nucleic acid sequence as shown in SEQ. ID NO:1.

2. The molecule of claim 1 wherein said hybridizing nucleic acid molecule hybridizes to SEQ. ID NO:1 under stringent conditions.

3. The molecule of claim 1 wherein said hybridizing nucleic acid molecule has at least 85% homology with a molecule having a nucleic acid sequence as shown in SEQ. ID NO:1.

4. The molecule of claim 1 wherein said hybridizing nucleic acid molecule has at least 90% homology with a molecule having a nucleic acid sequence as shown in SEQ. ID NO:1.

5. The molecule of claim 1 wherein said hybridizing nucleic acid molecule has at least 95% sequence identity with a molecule having a nucleic acid sequence as shown in SEQ. ID NO:1.

6. A DNA construct comprising the following operably linked elements:

a) a transcriptional promoter;

b) a DNA sequence including the nucleotide sequence as claimed in claim 2; and,

c) a transcriptional terminator.

7. A recombinant expression vector suitable for transformation of a host cell comprising a nucleic acid as claimed in claim 2 and a regulatory sequence operatively linked to said nucleic acid.

8. A transformed cell including a recombinant expression vector as claimed in claim 7.

9. A method for preparing an isolated amino acid sequence as claimed in claim 2, said method comprising culturing a transformed cell as claimed in claim 8 in a suitable medium until the protein is formed and isolating said protein.

10. The polypeptide expressed by the recombinant expression vector of claim 7.

11. A probe comprising an oligonucleotide of the nucleic acid as claimed in claim 2 capable of specifically hybridizing with a gene which encodes a protein having an amino acid sequence as shown in SEQ. ID. NO: 2 or allelic and species variants thereof.

12. A purified polyclonal antibody specific for the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof.

13. The purified polyclonal antibody of claim 12 wherein the antibody is specific for an extracellular epitope of the protein having the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof.

14. The purified polyclonal antibody of claim 12 wherein the antibody is labeled.

15. A monoclonal antibody specific for the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof.

16. The monoclonal antibody of claim 15 wherein said antibody is specific for an extracellular epitope of the protein having the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic varients thereof.

17. The monoclonal antibody of claim 15 wherein the antibody is labeled.

8. A transformed cell including a recombinant expression vector as claimed in claim 7.

9. A method for preparing an isolated amino acid sequence as claimed in claim 2, said method comprising culturing a transformed cell as claimed in claim 8 in a suitable medium until the protein is formed and isolating said protein.

10. The polypeptide expressed by the recombinant expression vector of claim 7.

11. A probe comprising an oligonucleotide of the nucleic acid as claimed in claim 2 capable of specifically hybridizing with a gene which encodes a protein having an amino acid sequence as shown in SEQ. ID. NO: 2 or allelic and species variants thereof.

12. A purified polyclonal antibody specific for the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof.

13. The purified polyclonal antibody of claim 12 wherein the antibody is specific for an extracellular epitope of the protein having the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof.

14. The purified polyclonal antibody of claim 12 wherein the antibody is labeled.

15. A monoclonal antibody specific for the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof.

16. The monoclonal antibody of claim 15 wherein said antibody is specific for an extracellular epitope of the protein having the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic varients thereof.

17. The monoclonal antibody of claim 15 wherein the antibody is labeled.

18. The method for determining the presence of a protein having an amino acid sequence as shown in SEQ. ID. NO: 2 or allelic variants thereof in a biological sample, the method comprising the steps of:

a) incubating the sample with amonoclonal antibody or purified polyclonal antibody which specifically binds to an epitope of said protein under conditions sufficient for the formation of an immune complex; and,

b) determining the presence of said immune complex.

19. The method of claim 18 wherein the monoclonal or purified polyclonal antibody is labeled.

20. A method of purifying a protein having the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic varients thereof, the method including an immunoaffinity chromatography process wherein a monoclonal antibody or a purified polyclonal antibody specific to an epitope of said protein is immobilized on the chromatography resin.

21. A method of screening a molecule which ligates to the protein having the amino acid sequence as shown in SEQ. ID. NO: 2 or allelic varients or fragments thereof comprising a signal transduction assay.

22. The method of claim 21, wherein the protein is a G protein coupled receptor, the method comprising the following steps:

a) co-transfecting into a suitable cell of a plasmid including a reporter gene and an expression plasmid coding for said protein;

b) expressing said protein;

c) treating said cell with serum starvation to reduce mitogenic activity;

d) applying said molecule which ligates to said protein in a serum free medium; and

e) measuring the activity of the reporter.

Figure 1

hedg-6 cDNA and predicted amino acid sequence. The cloning sites and poly(A) tail have been excluded from this figure.

Figure 1A
SEQ. ID NO:1

```
        CGCTCCCGCCGCAGTCGCCGGGCCATGGGCCTCGAGCCCGCCCCGAACCCCCGCGAGCCC
        GCGAGGGCGGCGTCAGCGGCCCGGTACCCGGAGCTCGGGCGGGGCTTGGGGGCGCTCGGG
      1 ---------+---------+---------+---------+---------+---------+    60
```

Figure 1B
SEQ. ID NO:2

```
                                        M  V  I  M  G  Q  C  Y  Y  N
        GCCTTGTCTGCGGCGTGACTGGAGGCCCAGATGGTCATCATGGGCCAGTGCTACTACAAC
        CGGAACAGACGCCGCACTGACCTCCGGGTCTACCAGTAGTACCCGGTCACGATGATGTTG
     61 ---------+---------+---------+---------+---------+---------+   120

        E  T  I  G  F  F  Y  N  N  S  G  K  E  L  S  S  H  W  R  P
        GAGACCATCGGTTTCTTCTATAACAACAGTGGCAAAGAGCTCAGCTCCCACTGGCGGCCC
        CTCTGGTAGCCAAAGAAGATATTGTTGTCACCGTTTCTCGAGTCGAGGGTGACCGCCGGG
    121 ---------+---------+---------+---------+---------+---------+   180

        K  D  V  V  V  V  A  L  G  L  T  V  S  V  L  V  L  L  T  N
        AAGGATGTGGTCGTGGTGGCACTGGGGCTGACCGTCAGCGTGCTGGTGCTGCTGACCAAT
        TTCCTACACCAGCACCACCGTGACCCCGACTGGCAGTCGCACGACCACGACGACTGGTTA
    181 ---------+---------+---------+---------+---------+---------+   240

        L  L  V  I  A  A  I  A  S  N  R  R  F  H  Q  P  I  Y  Y  L
        CTGCTGGTCATAGCAGCCATCGCCTCCAACCGCCGCTTCCACCAGCCCATCTACTACCTG
        GACGACCAGTATCGTCGGTAGCGGAGGTTGGCGGCGAAGGTGGTCGGGTAGATGATGGAC
    241 ---------+---------+---------+---------+---------+---------+   300

        L  G  N  L  A  A  A  D  L  F  A  G  V  A  Y  L  F  L  M  F
        CTCGGCAATCTGGCCGCGGCTGACCTCTTCGCGGGCGTGGCCTACCTCTTCCTCATGTTC
        GAGCCGTTAGACCGGCGCCGACTGGAGAAGCGCCCGCACCGGATGGAGAAGGAGTACAAG
```

```
301 ---------+---------+---------+---------+---------+---------+  360

    H  T  G  P  R  T  A  R  L  S  L  E  G  W  F  L  R  Q  G  L
    CACACTGGTCCCCGCACAGCCCGACTTTCACTTGAGGGCTGGTTCCTGCGGCAGGGCTTG
    GTGTGACCAGGGGCGTGTCGGGCTGAAAGTGAACTCCCGACCAAGGACGCCGTCCCGAAC
361 ---------+---------+---------+---------+---------+---------+  420

    L  D  T  S  L  T  A  S  V  A  T  L  L  A  I  A  V  E  R  H
    CTGGACACAAGCCTCACTGCGTCGGTGGCCACACTGCTGGCCATCGCCGTGGAACGGCAC
    GACCTGTGTTCGGAGTGACGCAGCCACCGGTGTGACGACCGGTAGCGGCACCTTGCCGTG
421 ---------+---------+---------+---------+---------+---------+  480

    R  S  V  M  A  V  Q  L  H  S  R  L  P  R  G  R  V  V  M  L
    CGCAGTGTGATGGCCGTACAGTTGCACAGCCGCCTGCCCCGTGGCCGCGTGGTCATGCTC
    GCGTCACACTACCGGCATGTCAACGTGTCGGCGGACGGGGCACCGGCGCACCAGTACGAG
481 ---------+---------+---------+---------+---------+---------+  540

    I  V  G  V  W  V  A  A  L  G  L  G  L  L  P  A  H  S  W  H
    ATTGTGGGCGTGTGGGTGGCTGCCCTGGGCCTGGGGCTGTTGCCTGCCCACTCCTGGCAC
    TAACACCCGCACACCCACCGACGGGACCCGGACCCCGACAACGGACGGGTGAGGACCGTG
541 ---------+---------+---------+---------+---------+---------+  600

    C  L  C  A  L  D  R  C  S  R  M  A  P  L  L  S  R  S  Y  L
    TGCCTCTGTGCCCTGGACCGCTGCTCACGCATGGCACCCCTGCTCAGCCGCTCCTATTTG
    ACGGAGACACGGGACCTGGCGACGAGTGCGTACCGTGGGGACGAGTCGGCGAGGATAAAC
601 ---------+---------+---------+---------+---------+---------+  660

    A  V  W  A  L  S  S  L  L  V  F  L  L  M  V  A  V  Y  T  R
    GCCGTCTGGGCTCTGTCGAGCCTGCTTGTCTTCCTGCTCATGGTGGCTGTGTACACCCGC
    CGGCAGACCCGAGACAGCTCGGACGAACAGAAGGACGAGTACCACCGACACATGTGGGCG
661 ---------+---------+---------+---------+---------+---------+  720
```

```
      I  F  L  Y  V  R  R  R  V  Q  R  M  A  E  H  V  S  C  H  P
      ATTTTTTTATACGTGCGGCGGCGAGTGCAGCGCATGGCAGAGCATGTCAGCTGCCACCCC
      TAAAAAAATATGCACGCCGCCGCTCACGTCGCGTACCGTCTCGTACAGTCGACGGTGGGG
721   ---------+---------+---------+---------+---------+---------+   780
      R  Y  R  E  T  T  L  S  L  V  K  T  V  V  I  I  L  G  A  F
      CGCTACCGAGAGACCACGCTCAGCCTGGTCAAGACTGTTGTCATCATCCTGGGGGCGTTC
      GCGATGGCTCTCTGGTGCGAGTCGGACCAGTTCTGACAACAGTAGTAGGACCCCCGCAAG
781   ---------+---------+---------+---------+---------+---------+   840

      V  V  C  W  T  P  G  Q  V  V  L  L  L  D  G  L  G  C  E  S
      GTGGTCTGCTGGACACCAGGCCAGGTGGTACTGCTCCTGGATGGTTTAGGCTGTGAGTCC
      CACCAGACGACCTGTGGTCCGGTCCACCATGACGAGGACCTACCAAATCCGACACTCAGG
841   ---------+---------+---------+---------+---------+---------+   900

      C  N  V  L  A  V  E  K  Y  F  L  L  L  A  E  A  N  S  L  V
      TGCAATGTCCTGGCTGTAGAAAAGTACTTCCTACTGTTGGCCGAGGCCAACTCACTGGTC
      ACGTTACAGGACCGACATCTTTTCATGAAGGATGACAACCGGCTCCGGTTGAGTGACCAG
901   ---------+---------+---------+---------+---------+---------+   960

      N  A  A  V  Y  S  C  R  D  A  E  M  R  R  T  F  R  R  L  L
      AATGCTGCTGTGTACTCTTGCCGAGATGCTGAGATGCGCCGCACCTTCCGCCGCCTTCTC
      TTACGACGACACATGAGAACGGCTCTACGACTCTACGCGGCGTGGAAGGCGGCGGAAGAG
961   ---------+---------+---------+---------+---------+---------+
1020

      C  C  A  C  L  R  Q  P  T  R  E  S  V  H  Y  T  S  S  A  Q
      TGCTGCGCGTGCCTCCGCCAGCCCACCCGCGAGTCTGTCCACTATACATCCTCTGCCCAG
      ACGACGCGCACGGAGGCGGTCGGGTGGGCGCTCAGACAGGTGATATGTAGGAGACGGGTC
1021  ---------+---------+---------+---------+---------+---------+
1080

      G  G  A  S  T  R  I  M  L  P  E  N  G  H  P  L  M  D  S  T
      GGAGGTGCCAGCACTCGCATCATGCTTCCCGAGAACGGCCACCCACTGATGGACTCCACC
```

```
        CCTCCACGGTCGTGAGCGTAGTACGAAGGGCTCTTGCCGGTGGGTGACTACCTGAGGTGG
  1081  ---------+---------+---------+---------+---------+---------+
1140

        L  *
        CTTTAGCTACCTTGAACTTCAGCGGTACGCGGCAAGCAACAAATCCACAGCCCCTGATGA
        GAAATCGATGGAACTTGAAGTCGCCATGCGCCGTTCGTTGTTTAGGTGTCGGGGACTACT
  1141  ---------+---------+---------+---------+---------+---------+
1200

        CTTGTGGGTGCTCCTGGCTCAACCCAACCAACAGGACTGACTGACCGGCAGGACAAGGTC
        GAACACCCACGAGGACCGAGTTGGGTTGGTTGTCCTGACTGACTGGCCGTCCTGTTCCAG
  1201  ---------+---------+---------+---------+---------+---------+
1260

        TGGCATGGCACAGCACCACTGCCAGGCCTCCCCAGGCACACCACTCTGCCCAGGGAATGG
        ACCGTACCGTGTCGTGGTGACGGTCCGGAGGGGTCCGTGTGGTGAGACGGGTCCCTTACC
  1261  ---------+---------+---------+---------+---------+---------+
1320

        GGGCTTTGGGTCATCTCCCACTGCCTGGGGGAGTCAGATGGGGTGCAGGAATCTGGCTCT
        CCCGAAACCCAGTAGAGGGTGACGGACCCCCTCAGTCTACCCCACGTCCTTAGACCGAGA
  1321  ---------+---------+---------+---------+---------+---------+
1380

        TCAGCCATCCCAGGTTTAGGGGGTTTGTAACAGACATTATTCTGTTTTCACTGCGTATCC
        AGTCGGTAGGGTCCAAATCCCCCAAACATTGTCTGTAATAAGACAAAAGTGACGCATAGG
  1381  ---------+---------+---------+---------+---------+---------+
1440

        TTGGTAAGCCCTGTGGACTGGTTCCTGCTGTGTGATGCTGAGGGTTTTAAGGTGGGGAGA
        AACCATTCGGGACACCTGACCAAGGACGACACACTACGACTCCCAAAATTCCACCCCTCT
```

```
   1441  ---------+---------+---------+---------+---------+---------+
1500

        GATAAGGGCTCTCTCGGGCCATGCTACCCGGTATGACTGGGTAATGAGGACAGACTGTGG
        CTATTCCCGAGAGAGCCCGGTACGATGGGCCATACTGACCCATTACTCCTGTCTGACACC
   1501  ---------+---------+---------+---------+---------+---------+
1560

        ACACCCCATYTACCTGAGTCTGATTCTTTAGCAGCAGAGACTGAGGGGTGCAGAGTGTGA
        TGTGGGGTARATGGACTCAGACTAAGAAATCGTCGTCTCTGACTCCCCACGTCTCACACT
   1561  ---------+---------+---------+---------+---------+---------+
1620

        GCTGGGAAAGGTTTGTGGCTCCTTGCAGCCTCCAGGGACTGGCCTGTCCCCGATAGAATT
        CGACCCTTTCCAAACACCGAGGAACGTCGGAGGTCCCTGACCGGACAGGGGCTATCTTAA
   1621  ---------+---------+---------+---------+---------+---------+
1680

        GAAGCAGTCCACGGGGAGGGGATGATACAAGGAGTAAACCTTTCTTTACACTCTGAGGTC
        CTTCGTCAGGTGCCCCTCCCCTACTATGTTCCTCATTTGGAAAGAAATGTGAGACTCCAG
   1681  ---------+---------+---------+---------+---------+---------+
1740

        TCCAAAACATTTGTTGTTATC
        AGGTTTTGTAAACAACAATAG
   1741  ---------+---------+-  1761
```

Figure 2

Nucleotide sequence of human edg-6 cDNA insert. Sequence includes the EcoRI (position 81) and NotI (position 1882) cloning sites and the 34 bp poly(A) tail

SEQ. ID NO:3

```
      TTACGAATTAATACGATCACTATAGGGAGACCAAGCTTGGTACCGAGCTCGGATCCACTA
    1 ---------+---------+---------+---------+---------+---------+   60

      GTAACGGCCGCCAGTGTGGGGAATTCCGCTCCCGCCGCAGTCGCCGGGCCATGGGCCTCG
   61 ---------+---------+---------+---------+---------+---------+  120

      AGCCCGCCCCGAACCCCCGCGAGCCCGCCTTGTCTGCGGCGTGACTGGAGGCCCAGATGG
  121 ---------+---------+---------+---------+---------+---------+  180

      TCATCATGGGCCAGTGCTACTACAACGAGACCATCGGTTTCTTCTATAACAACAGTGGCA
  181 ---------+---------+---------+---------+---------+---------+  240

      AAGAGCTCAGCTCCCACTGGCGGCCCAAGGATGTGGTCGTGGTGGCACTGGGGCTGACCG
  241 ---------+---------+---------+---------+---------+---------+  300

      TCAGCGTGCTGGTGCTGCTGACCAATCTGCTGGTCATAGCAGCCATCGCCTCCAACCGCC
  301 ---------+---------+---------+---------+---------+---------+  360

      GCTTCCACCAGCCCATCTACTACCTGCTCGGCAATCTGGCCGCGGCTGACCTCTTCGCGG
  361 ---------+---------+---------+---------+---------+---------+  420

      GCGTGGCCTACCTCTTCCTCATGTTCCACACTGGTCCCCGCACAGCCCGACTTTCACTTG
  421 ---------+---------+---------+---------+---------+---------+  480

      AGGGCTGGTTCCTGCGGCAGGGCTTGCTGGACACAAGCCTCACTGCGTCGGTGGCCACAC
  481 ---------+---------+---------+---------+---------+---------+  540

      TGCTGGCCATCGCCGTGGAACGGCACCGCAGTGTGATGGCCGTACAGTTGCACAGCCGCC
  541 ---------+---------+---------+---------+---------+---------+  600

      TGCCCCGTGGCCGCGTGGTCATGCTCATTGTGGGCGTGTGGGTGGCTGCCCTGGGCCTGG
  601 ---------+---------+---------+---------+---------+---------+  660

      GGCTGTTGCCTGCCCACTCCTGGCACTGCCTCTGTGCCCTGGACCGCTGCTCACGCATGG
  661 ---------+---------+---------+---------+---------+---------+  720

      CACCCCTGCTCAGCCGCTCCTATTTGGCCGTCTGGGCTCTGTCGAGCCTGCTTGTCTTCC
  721 ---------+---------+---------+---------+---------+---------+  780

      TGCTCATGGTGGCTGTGTACACCCGCATTTTTTTATACGTGCGGCGGCGAGTGCAGCGCA
  781 ---------+---------+---------+---------+---------+---------+  840

      TGGCAGAGCATGTCAGCTGCCACCCCCGCTACCGAGAGACCACGCTCAGCCTGGTCAAGA
  841 ---------+---------+---------+---------+---------+---------+  900

      CTGTTGTCATCATCCTGGGGGCGTTCGTGGTCTGCTGGACACCAGGCCAGGTGGTACTGC
  901 ---------+---------+---------+---------+---------+---------+  960

      TCCTGGATGGTTTAGGCTGTGAGTCCTGCAATGTCCTGGCTGTAGAAAAGTACTTCCTAC
  961 ---------+---------+---------+---------+---------+---------+ 1020

      TGTTGGCCGAGGCCAACTCACTGGTCAATGCTGCTGTGTACTCTTGCCGAGATGCTGAGA
 1021 ---------+---------+---------+---------+---------+---------+ 1080

      TGCGCCGCACCTTCCGCCGCCTTCTCTGCTGCGCGTGCCTCCGCCAGCCCACCCGCGAGT
 1081 ---------+---------+---------+---------+---------+---------+ 1140
```

```
      CTGTCCACTATACATCCTCTGCCCAGGGAGGTGCCAGCACTCGCATCATGCTTCCCGAGA
1141  ---------+---------+---------+---------+---------+---------+  1200

      ACGGCCACCCACTGATGGACTCCACCCTTTAGCTACCTTGAACTTCAGCGGTACGCGGCA
1201  ---------+---------+---------+---------+---------+---------+  1260
      AGCAACAAATCCACAGCCCCTGATGACTTGTGGGTGCTCCTGGCTCAACCCAACCAACAG
1261  ---------+---------+---------+---------+---------+---------+  1320

      GACTGACTGACCGGCAGGACAAGGTCTGGCATGGCACAGCACCACTGCCAGGCCTCCCCA
1321  ---------+---------+---------+---------+---------+---------+  1380

      GGCACACCACTCTGCCCAGGGAATGGGGGCTTTGGGTCATCTCCCACTGCCTGGGGGAGT
1381  ---------+---------+---------+---------+---------+---------+  1440

      CAGATGGGGTGCAGGAATCTGGCTCTTCAGCCATCCCAGGTTTAGGGGGTTTGTAACAGA
1441  ---------+---------+---------+---------+---------+---------+  1500

      CATTATTCTGTTTTCACTGCGTATCCTTGGTAAGCCCTGTGGACTGGTTCCTGCTGTGTG
1501  ---------+---------+---------+---------+---------+---------+  1560

      ATGCTGAGGGTTTTAAGGTGGGGAGAGATAAGGGCTCTCTCGGGCCATGCTACCCGGTAT
1561  ---------+---------+---------+---------+---------+---------+  1620

      GACTGGGTAATGAGGACAGACTGTGGACACCCCATYTACCTGAGTCTGATTCTTTAGCAG
1621  ---------+---------+---------+---------+---------+---------+  1680

      CAGAGACTGAGGGGTGCAGAGTGTGAGCTGGGAAAGGTTTGTGGCTCCTTGCAGCCTCCA
1681  ---------+---------+---------+---------+---------+---------+  1740

      GGGACTGGCCTGTCCCCGATAGAATTGAAGCAGTCCACGGGGAGGGGATGATACAAGGAG
1741  ---------+---------+---------+---------+---------+---------+  1800

      TAAACCTTTCTTTACACTCTGAGGTCTCCAAAACATTTGTTGTTATCAAAAAAAAAAAAA
1801  ---------+---------+---------+---------+---------+---------+  1860

      AAAAAAAAAAAAAAAAAAAAAAGCGGCCGC
1861  ---------+---------+---------  1889
```

INTERNATIONAL SEARCH REPORT

Interr. nal Application No
PCT/CA 98/00487

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/705 C12N5/10 C07K16/28 G01N33/563
G01N33/50 A61K31/70 A01K67/00

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K C12N G01N A61K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 30406 A (CAO LIANG ;HUMAN GENOME SCIENCES INC (US); LI YI (US); NI JIAN (US) 3 October 1996	1-4,6-8, 10-27,31
Y	see the whole document	28-30
Y	WO 97 00952 A (INCYTE PHARMA INC) 9 January 1997 see the whole document	28-30
A	HECHT J H ET AL: "VENTRICULAR ZONE GENE-1 (VZG-1) ENCODES A LYSOPHOSPHATIDIC ACID RECEPTOR EXPRESSED IN NEUROGENIC REGIONS OF THE DEVELOPING CEREBRALCORTEX" THE JOURNAL OF CELL BIOLOGY, vol. 135, no. 4, November 1996, pages 1071-1083, XP002046888 cited in the application see the whole document	1-36

-/--

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 October 1998	27/10/1998

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Interr nal Application No
PCT/CA 98/00487

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	AN S ET AL: "MOLECULAR CLONING OF THE HUMAN EDG2 PROTEIN AND ITS IDENTIFICATION AS A FUNCTIONAL CELLULAR RECEPTOR FOR LYSOPHOSPHATIDIC ACID" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 231, no. 3, 24 February 1997, pages 619-622, XP002046899 cited in the application see the whole document ---	1-36
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E	EP 0 855 443 A (SMITHKLINE BEECHAM CORP) 29 July 1998 see the whole document -----	1-29,31

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INTERNATIONAL SEARCH REPORT

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International Application No
PCT/CA 98/00487

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